

Remarks

A. *Status of Claims*

Applicants have not amended the claims. Claims 19-35 remain pending and are listed above for the Examiner's convenience. The Office has indicated that claims 23 and 32-35 contain allowable subject matter.

B. *Section 103 Rejections*

Claims 24-31 stand rejected under 35 U.S.C. § 103 as being obvious in view of U.S. Patent No. 5,922,537 ("Ewart") combined with U.S. Patent No. 6,149,789 ("Benecke"). Applicants respectfully traverse.

Claim 24 requires a specific type of microparticle—one having (a) a conductive core, (b) an insulating layer coating the core and having a thickness sufficient to render the engineered microparticle maneuverable by dielectrophoresis, and (c) a linking element. That particular microparticle must be associated with a target analyte to form a complex. That complex must then be manipulated using dielectrophoresis. The Office argues that Ewart discloses all the features except for dielectrophoresis manipulation, which Benecke purportedly shows. The Office, however, has not established a *prima facie* case of obviousness.

To establish a *prima facie* case of obviousness, there must first be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. *See* M.P.E.P. §2142. The initial burden is on the Examiner to provide some suggestion of the desirability of doing what the inventors have done. *Id.* The mere fact that references *can* be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. *See* M.P.E.P. §2143.01. If the proposed modification or

combination of the prior art would change the principle of operation of the prior art invention being modified, then the teachings of the references are not sufficient to render the claims *prima facie* obvious. *Id.*

Here, the Office cannot meet the initial burden of showing a suggestion or motivation to combine Ewart with Benecke. Neither Ewart nor Benecke suggest or motivate the combination being proposed by the Office. Particularly, Ewart nowhere suggests or motivates any dielectrophoretic manipulation. Ewart has no need for such manipulation, so its lack of disclosure, suggestion, or motivation is understandable. Ewart is directed to techniques in which analytes compete with one another to displace a reporter particle off a test surface. *See* Ewart, col. 4, lines 35-42. When a reporter leaves the test surface, the capacitance of the test surface is changed and can be measured to indicate an analyte. *Id.* Nowhere in this process, or any other process described in Ewart, is it suggested that dielectrophoretic manipulation would be helpful or should even be considered. Nor is it clear how dielectrophoretic manipulation could even be applied to Ewart, given that the “displacement” in Ewart stems from competing analytes, not displacement set up by a field sufficient to effect dielectrophoretic manipulation. Moreover, to the extent that the Ewart could be modified to incorporate dielectrophoretic manipulation, its introduction would clearly change the principle of operation of Ewart, which confirms that there is no *prima facie* case of obviousness. Specifically, if dielectrophoretic manipulation were used instead of the analyte-competition mechanism to displace reporter particles to and from a test surface, Ewart’s entire principle of operation (competition-based displacement) would be altered. Again, Ewart provides no motivation or suggestion to do so.

Benecke likewise does not offer any motivation or suggestion to combine the art as proposed by the Office. Benecke is cited for the general proposition that certain dielectric

particles can be manipulated using dielectrophoresis. *See* Office Action, p. 2. However, the fact that dielectric particles can be manipulated by dielectrophoresis (e.g. just because aspects of Benecke arguably *can* be combined with Ewart) does not justify an obviousness rejection. Benecke, like Ewart, nowhere suggests the desirability of manipulating the specific type of microparticle¹ and target analyte required by claim 24—one having a conducting core, a particular insulating coating, and a linking element, which are then associated with the target analyte. Instead, Benecke simply reinforces that electric fields can be used to influence dielectric particles. *See* Benecke, col. 1, lines 61-67 (cited by the Office).

The Office's justifies combining the references by stating:

It would have been obvious ... to use the method of Benecke to manipulate dielectric particles such as those of Ewart in an assay for detecting analyte as taught by Ewart. Since Ewart suggests using dielectric particles in assay and it is known in the art that dielectrophoresis is used for manipulating dielectric particles, one of ordinary skills in the art would find it obvious to manipulate the dielectric particles via dielectrophoresis.

Office Action, p. 2. This justification does not meet the initial burden for showing a *prima facie* case. Nowhere has the Office objectively established why Ewart or Benecke suggest or motivate the dielectrophoretic manipulation of the particles of Ewart. As explained above, Ewart does not require or suggest such manipulation and, importantly, such manipulation would change its operating principle. Benecke, just by disclosing that dielectric particles can be manipulated, does not motivate or suggest the manipulation of the particular particles recited in claim 24 (or the

¹ It is Applicants' position that Ewart does not disclose or suggest the particular microparticle of claim 24, but Applicants have focused their arguments on the lack of any motivation to combine the cited references and a lack of any showing that there would be a reasonable expectation of success. In Applicants' opinion, the lack of motivation and lack of reasonable success is readily apparent and therefore represents an efficient, concise rebuttal of the Office's rejection, which shows that the claims are allowable. Applicants reserve the right to raise arguments concerning the microparticle (and, generally, prong three of the *prima facie* requirements, if needed.

particles of Ewart). Moreover, the Office has not provided evidence why someone of ordinary skill in the art would be motivated to combine the references, given that neither reference suggests, motivates, or requires the change being proposed by the Office. In sum, the Office's observation amounts to an allegation that the invention is within the capabilities of one of ordinary skill in the art. The Board of Patent Appeals and Interferences, however, has held that the fact that the claimed invention is within the capabilities of one of ordinary skill in the art is not sufficient by itself to establish obviousness. *Ex parte Levengood*, 28 U.S.P.Q.2d 1300 (BPAI 1993). Section 2143.01 of the M.P.E.P. explains the *Levengood* holding as follows:

A statement that modifications of the prior art to meet the claimed invention would have been "well within the ordinary skill of the art at the time the claimed invention was made" because the references relied upon teach that all aspects of the claimed invention were individually known in the art is not sufficient to establish a *prima facie* case of obviousness without some objective reason to combine the teachings of the references.

M.P.E.P. §2143.01.

The second prong of any *prima facie* case for obviousness involves a showing that there is a reasonable expectation of success. See M.P.E.P. §2142. Here, the Office has not provided evidence that would suggest that the combination of Ewart and Benecke would enjoy such a reasonable expectation of success. If Ewart were combined with Benecke, one would arguably need to construct electrodes or other mechanisms to generate an electric field sufficient to effect dielectrophoretic manipulation; however, nowhere do the references indicate or suggest how that would be done, especially given that Ewart already makes use of a test sensor surface whose capacitance is being measured for slight changes. Likewise, nothing in Benecke indicates that electric fields mentioned in Benecke would be sufficient to manipulate the particles disclosed in Ewart via dielectrophoresis. In particular, there is no guidance concerning, for example, the field

strength or field frequencies that would work to yield particle manipulation. For this reason as well, there is no *prima facie* case.

In view of at least the above arguments, Applicants respectfully request removal of the present rejection so that claims 24-31 can pass to issuance along with the claims that have already been indicated to contain allowable subject matter.

C. *Section 102 Rejections*

Claims 19, 20, and 22 remain rejected under 35 U.S.C. § 102(b) as being anticipated by Ewart. Applicants respectfully traverse.

Applicants argued at length during the last response why Ewart does not disclose or suggest the requirements of claims 19, 20, and 22. Those arguments still apply and are incorporated into this response by reference. The Office considered the arguments and responded as follows:

The changes in capacitance in Ewart are equivalent to the differences in dielectric properties thus satisfies the requirement of the present invention. Ewart teaches that the change [in capacitance] is determined exclusively by the change in dielectric constant of the particles to the dielectric constant of water in the **complexing layer** (emphasis added). The complexing layer of the present invention fails to exclude water as part of the complex. In fact, the sample of the present invention includes blood, saliva, which consists of some water. Since Ewart discloses the same methods with similar reagents as those of the present invention, the results of the two methods would be the same.

Office Action, p. 5 (emphasis in original).

Applicants believe that the Office's assertions indicate a possible misunderstanding about how Applicants are using the phrase "complex" in claim 19, which, if clarified, highlights that claim 19 and its dependent claims are allowable. In claim 19, the "complex" is the particular, engineered microparticle associated with a target analyte (*i.e.*, it is the **combination** of the particle + target). In claim 19, the complex is detected by distinguishing the dielectric property of the microparticle (alone) with the dielectric property of the combined particle plus target. In

Ewart, in stark contrast, a change in capacitance is being determined exclusively by a change in dielectric constant of particles to the dielectric constant of water, as recognized by the Office.

Put into a more graphical format:

Applicants' invention detection mechanism	Ewart detection mechanism
<i>dielectric property difference between:</i> particular microparticle vs. (particular microparticle + target)	<i>change in capacitance between:</i> particle vs. water

As acknowledged by the Office, claim 19 does not preclude a target or “complex” from containing water. However, even if that were the case, claim 19 would still involve the distinguishing of dielectric properties of microparticle vs. (microparticle + water-containing target), while Ewart still exclusively involves the change in capacitance arising from particle vs. water (alone).

This admitted difference, when viewed in the light of the clarified term “complex,” objectively demonstrates that Ewart does not disclose or even suggest the explicitly-required elements of claim 19. Instead, Ewart involves a different technique that does not take advantage of the dielectric property differences between a particular microparticle and the combination of that microparticle with a target (*i.e.* a “complex”).

For at least these reasons, Applicants respectfully request the Office to reconsider its previous statements and favorably judge claims 19 and all of its dependent claims as being allowable over the art of record. Applicants respectfully submit that the differences between Applicants' techniques and those of Ewart, such as those highlighted here by example, represent patentable distinctions. Accordingly, a notice of allowance is requested so that all the claims can issue together without the need for an appeal or further proceedings.

Petition for Extension of Time

Pursuant to 37 C.F.R. § 1.136(a), Applicants petition for an extension of time of one month up to and including December 15, 2003, in which to respond to the Office Action dated August 13, 2003. A check for the \$55.00 extension fee is enclosed. Should any additional fees be required for any reason, or should an over-payment be included, the Commissioner is authorized to deduct or credit Fulbright & Jaworski Deposit Account No. 50-1212/UTXC:626US/MCB.

Conclusion

Applicants believe this response fully and completely addresses all outstanding issues for this application. Applicants respectfully submit that the rejections of all pending claims should be withdrawn. If the Examiner intends to maintain any of the rejections discussed in this response, the courtesy of a telephone conference between the Examiner, the Examiner's supervisor, and the undersigned attorney is respectfully requested in advance to more efficiently resolve matters.

Respectfully submitted,

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